Variations of X chromosome inactivation occur in early passages of female human embryonic stem cells.

Journal: PLoS One

Publication Year: 2010

Authors: Tamar Dvash, Neta Lavon, Guoping Fan

PubMed link: 20593031

Funding Grants: Epigenetic gene regulation during the differentiation of human embryonic stem cells: Impact on neural repair

Public Summary:

Scientific Abstract:
X chromosome inactivation (XCI) is a dosage compensation mechanism essential for embryonic development and cell physiology. Human embryonic stem cells (hESCs) derived from inner cell mass (ICM) of blastocyst stage embryos have been used as a model system to understand XCI initiation and maintenance. Previous studies of undifferentiated female hESCs at intermediate passages have shown three possible states of XCI; 1) cells in a pre-XCI state, 2) cells that already exhibit XCI, or 3) cells that never undergo XCI even upon differentiation. In this study, XCI status was assayed in ten female hESC lines between passage 5 and 15 to determine whether XCI variations occur in early passages of hESCs. Our results show that three different states of XCI already exist in the early passages of hESC. In addition, we observe one cell line with skewed XCI and preferential expression of X-linked genes from the paternal allele, while another cell line exhibits random XCI. Skewed XCI in undifferentiated hESCs may be due to clonal selection in culture instead of non-random XCI in ICM cells. We also found that XIST promoter methylation is correlated with silencing of XIST transcripts in early passages of hESCs, even in the pre-XCI state. In conclusion, XCI variations already take place in early passages of hESCs, which may be a consequence of in vitro culture selection during the derivation process. Nevertheless, we cannot rule out the possibility that XCI variations in hESCs may reflect heterogeneous XCI states in ICM cells that stochastically give rise to hESCs.